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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,893	02/27/2006	Jean Pierre Plouet	0508-1134	2413

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
05/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,893	PLOUET ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *31 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 31, 2009 has been entered.

2. Claim 36 is pending and under examination in the instant application.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 257) in view of Concina et al (J Vasc Res. 2000 May-Jun;37(3):202-8).

Saito et al teach a method for the production of monoclonal antibodies reactive with tumor vasculature by immunization of mice with angiogenic factor-induced human umbilical vein endothelial cells (see title in particular). Saito et al teach that the development of new vessels, a phenomenon called angiogenesis, is essential for the development and progression of cancer and consequently, inhibition of angiogenesis may be an effective strategy for the treatment of cancer. Targeting of tumor vasculature using monoclonal antibodies (Mabs) may be an effective approach to inhibit angiogenesis, and for this purpose, the development of monoclonal antibodies reactive specifically with tumor vascular endothelial cells is necessary. One of the most important restrictions for the clinical application of these antibodies is the reactivity with normal vasculature as well as with other normal cells. In an attempt to produce Mabs specific for angiogenic endothelium, we immunized mice with human umbilical vein endothelial cells (HUVECs) stimulated wit angiogenic factors, namely vascular-endothelial growth factor

(VEGF), basic fibroblast growth factor (bFGF), and EEP, a growth factor obtained from new-born bovine brains added wit murine epidermal growth factor and heparin. With this approach, we obtained several monoclonal antibodies reactive wit HUVECs. Among them, some were confirmed to be specifically reactive wit tumor vasculature, by immunohistochemistry of frozen-sections of colon cancer and normal colonic mucosa. Neither endothelium of normal colonic mucosa nor the normal blood cells reacted with these Mabs (see abstract).

Saito et al reference teachings differ from the claimed invention only in the recitation that the angiogenic phenotype being obtained by culturing endothelial cells removed from an aorta in a medium containing a supplement consisting essentially of oestradiol and VEGF in claim 36.

However, Concina et al teaches the mitogenic effect of 17B-Estradiol (E2, i.e. claimed oestradiol) on *in vitro* endothelial cell proliferation and on *in vivo* reendotheliazation are both dependent on vascular endothelial growth factor (VEGF) (see title). Concina et al teach uses foetal bovine aortic endothelia cells (FBAEC) to study the action of estradiol. Concina et al teach that thoratic aorta VEGF content was increased in E-2-treated rats compared to control rats (see abstract). Concina et al teach VEGF quantification in the conditioned media of FBAEC revealed that E2 was able to induce VEGF synthesis in a dose-dependent fashion (see page 204, 2nd col., last sentence, and Fig. 3). Fig. 3 shows the effect of E2 on VEGF content in conditioned medium of FBAEC, wherein FBAEC were incubated with E2 for 48hrs. Concina et al teach that it cannot be excluded that E2 might act on the recently described endothelial cell progenitors which express VEGFR2 and become incorporated into sites of active angiogenesis. The enhancement of endothelium-derived nitric oxide bioactivity by E2 could contribute to potentiate the VEGF-dependent proliferation of the macrovascular endothelium (see page 207, 2nd col., last ¶).

It would have been obvious to one skilled in the art at the time the invention was made to immune the E2-treated FBAEC which induce VEGF synthesis taught by Concina et al in a method of producing monoclonal antibodies reactive with tumor vasculature taught by Saito et al.

Those of skill in the art would have had reason to use the FBAEC taught by Concina et al as a substitute for the immunization of mice taught in Saito et al because, like the HUEVC taught in Saito et al, FBAEC cell have angiogenic phenotype. Substituting a known element for another, to yield the known result, is obvious. *See KSR*, 550 U.S. at 416, 421.

It has been held that "[W]hen a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result." *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 416 (2007).

"When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." Id at 421.

While the prior art teachings may be silent as to the specific angiogenic phenotype recited in the claim; the method, the aortic endothelial cells and the culturing conditions (oestradiol and VEGF) used in the reference method are the same as the claimed method. Therefore the claimed angiogenic phenotype is considered inherent properties.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 20, 2009

/Maher M. Haddad/
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Primary Examiner
Technology Center 1600